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Transmissible spongiform encephalopathies: TSE Conformers

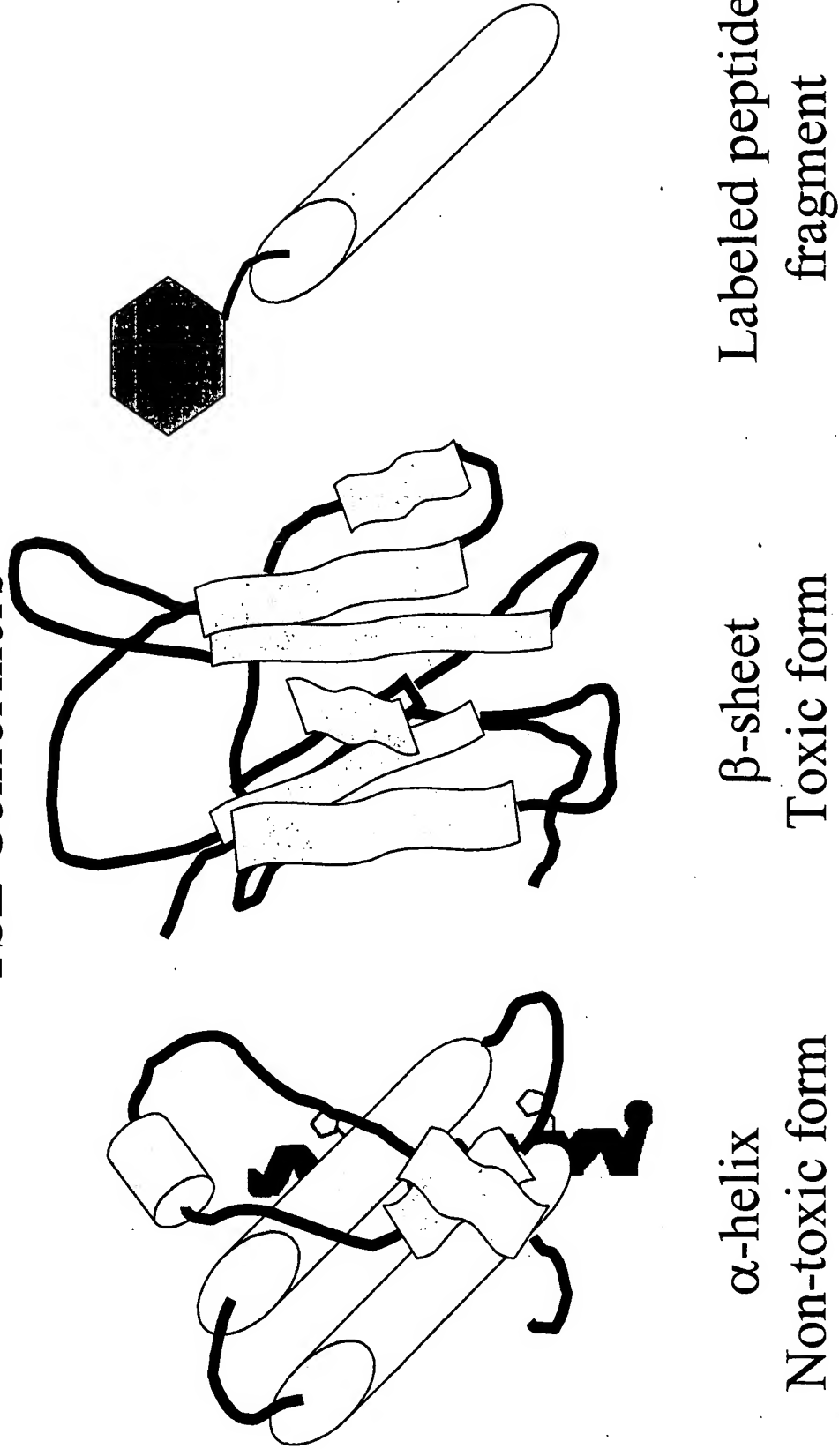


Figure 1

TSE Detection Schema

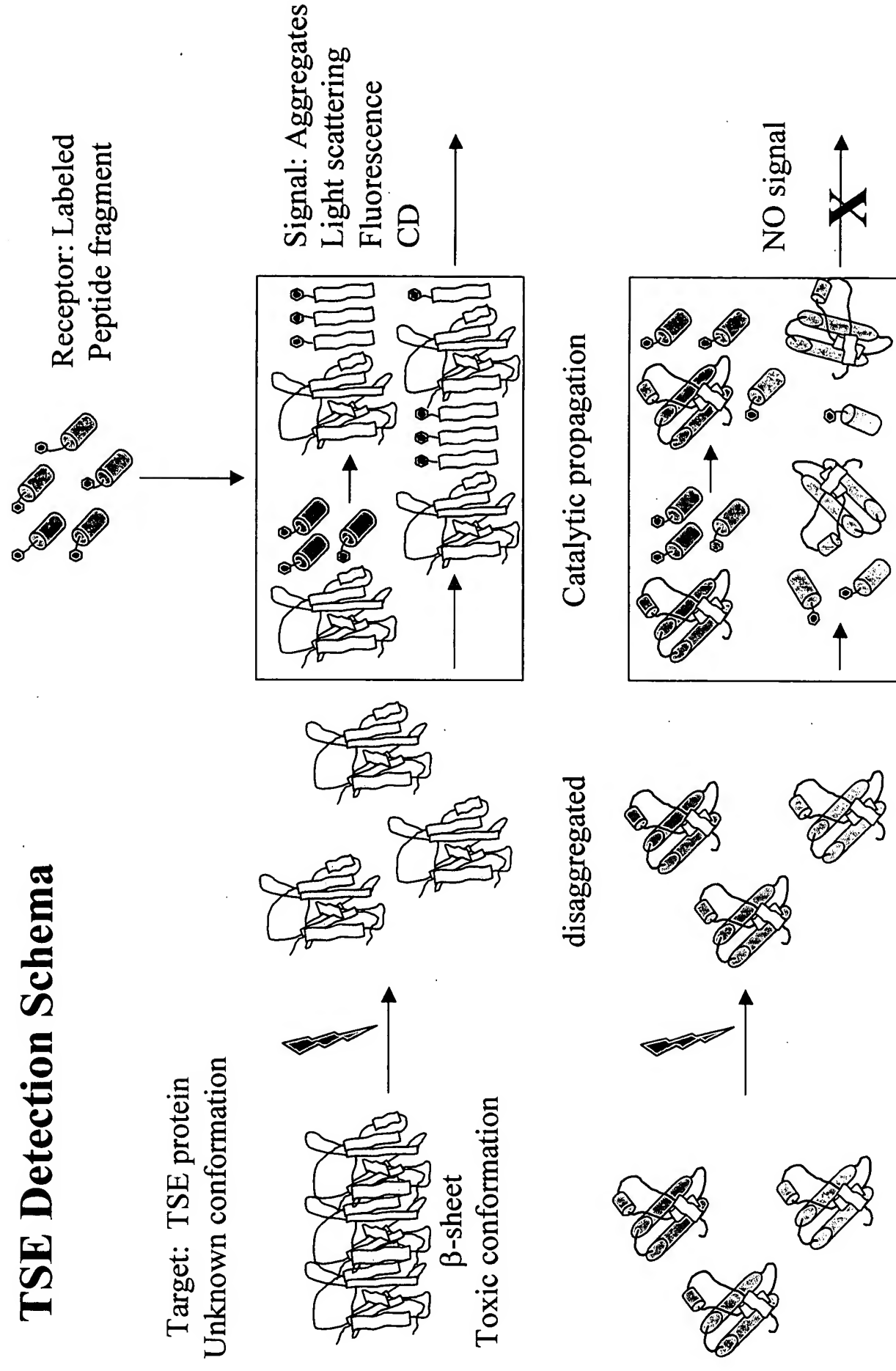


Figure 2

Circular Dichroism Indicating Conformational Change

Poly-L-Lysine 20 μ M 52,000 MW

Initial test peptide system

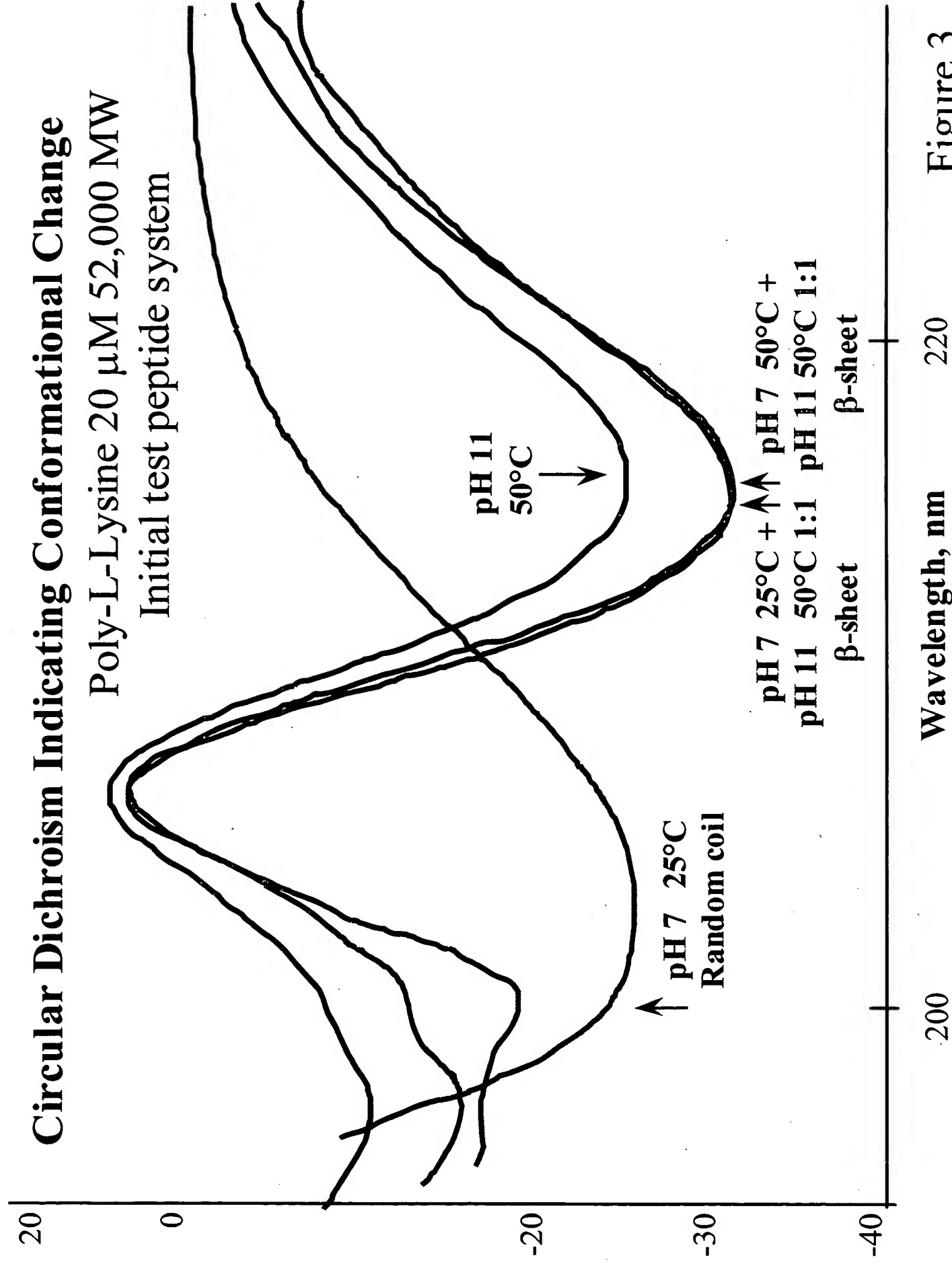


Figure 3

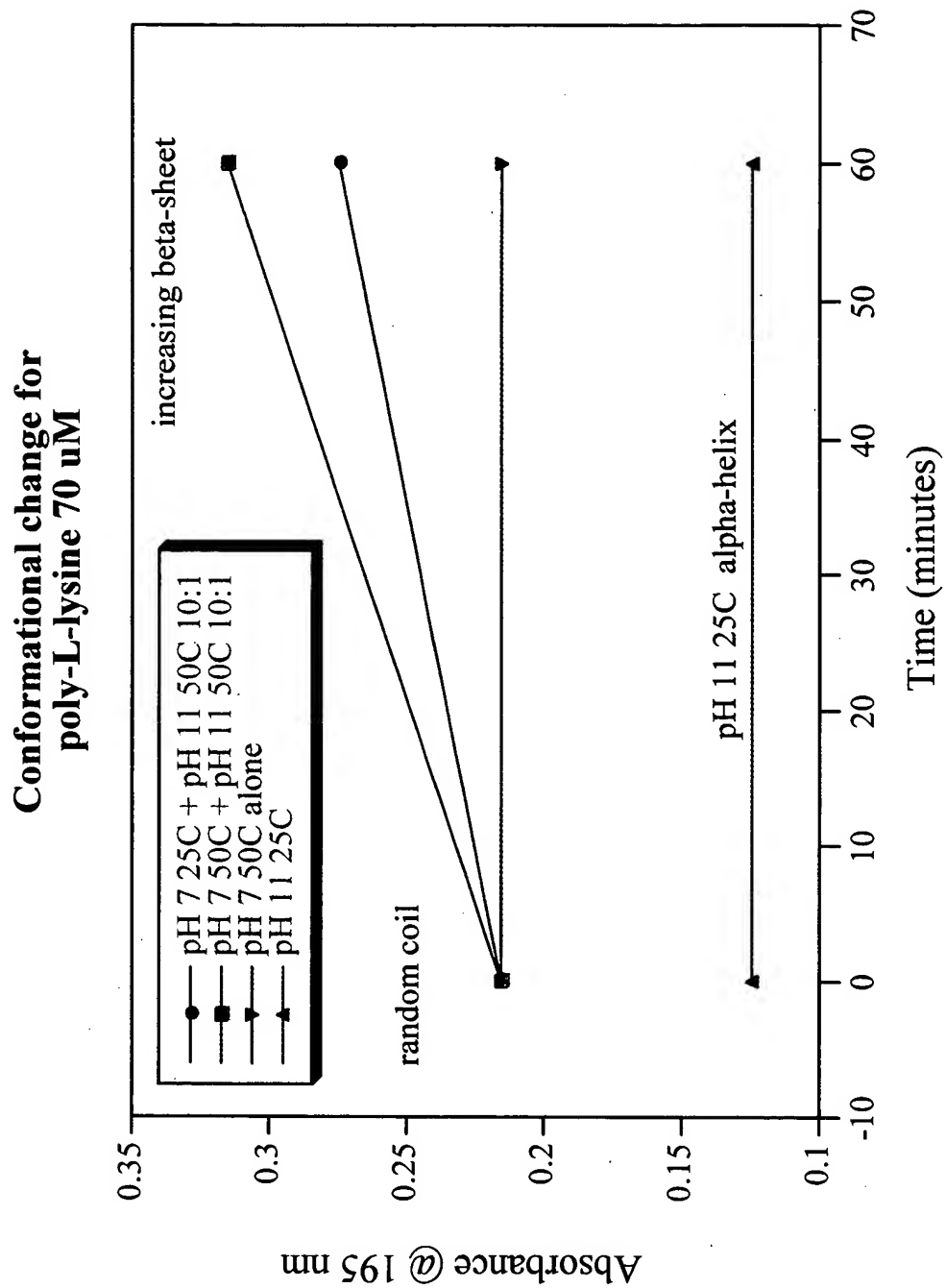


Figure 4

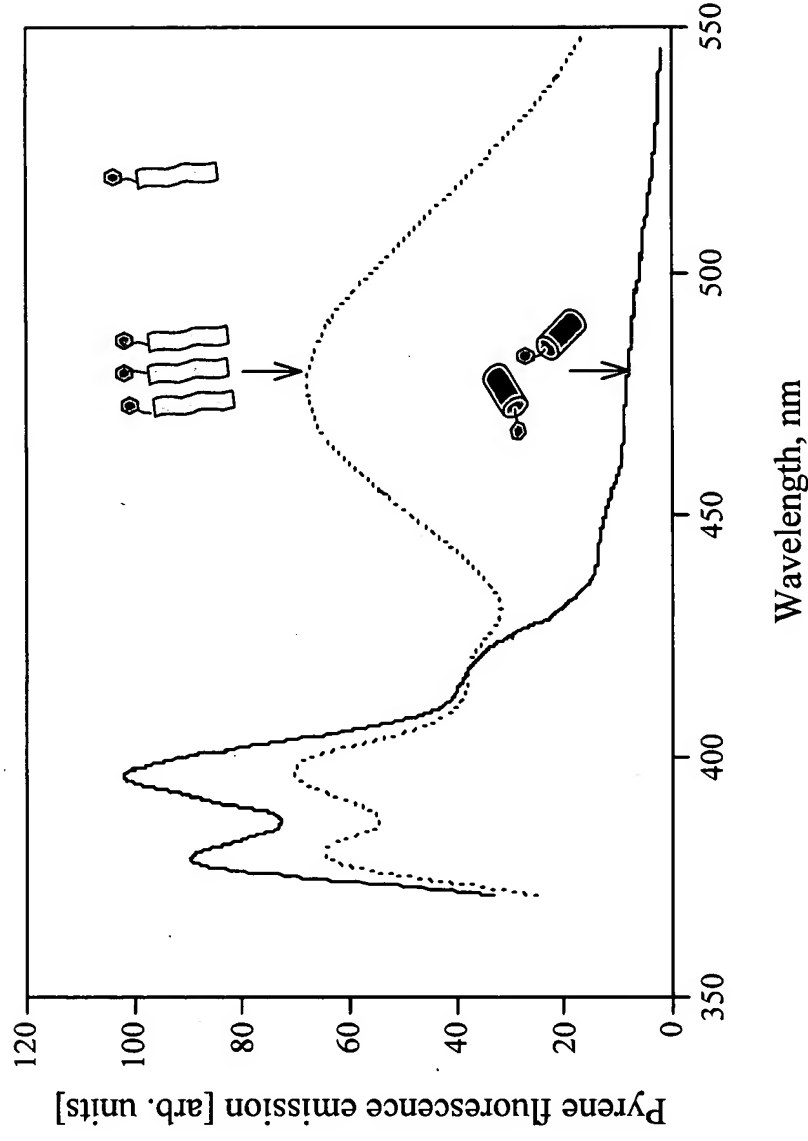
Circular Dicroism (CD) of Poly-L- Lysine varying Temp and pH

Temperature °C	25°C	50°C
pH 7 alone	Random coil	Random coil
pH 11 alone	α -helix	β -sheet
pH 7 + pH 11	β -sheet	β -sheet
pH 11 25°C + pH 11 50°C	Random coil	-----

Figure 5

Experiments with fluorescent probes for detection.

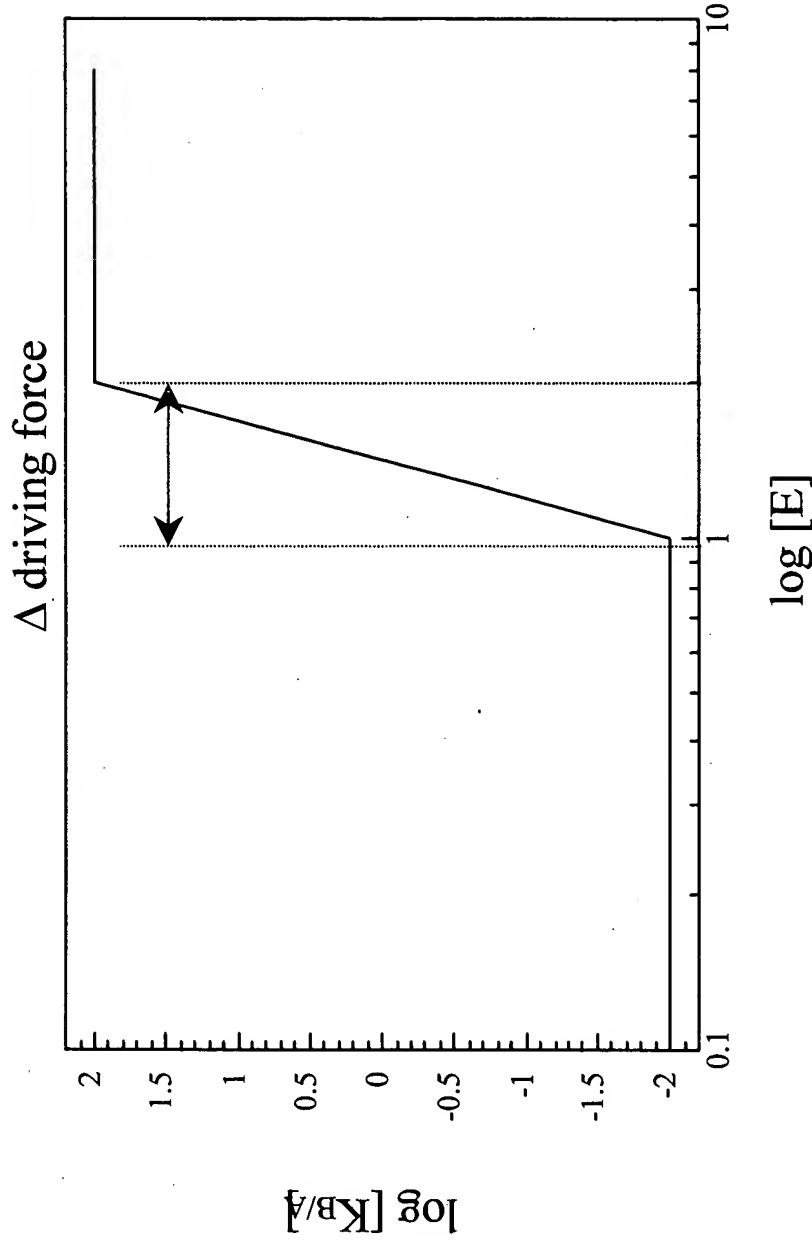
The data are from previous FRET experiments for proximal and distal locations in an α -helical bundle structure undergoing **conformational change**.



The spectra shown are for pyrene excimer formation at 480 nm, but other probes (FITC, etc.) can be used.

Figure 6

Engineering considerations for sensor design



The **driving force** must be commensurate with the **energetic difference** between the two conformational states

The process is driven by a **differential interaction** of the target peptide E, with the two conformations of the test PrP molecule.

Figure 7

Figure 8

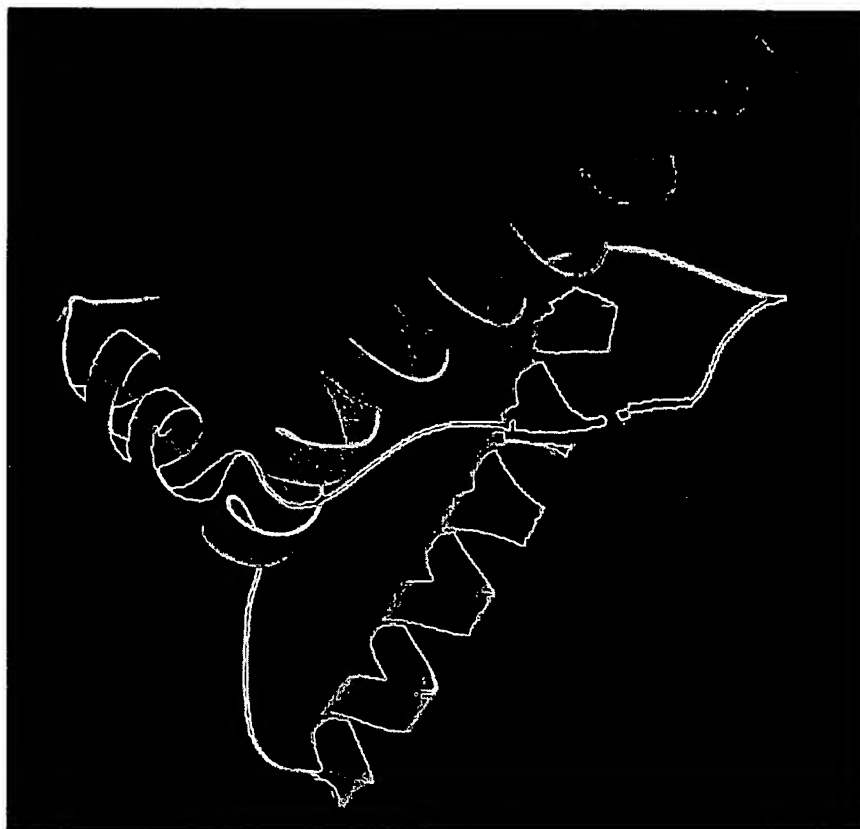


Figure 9



FIGURE 10

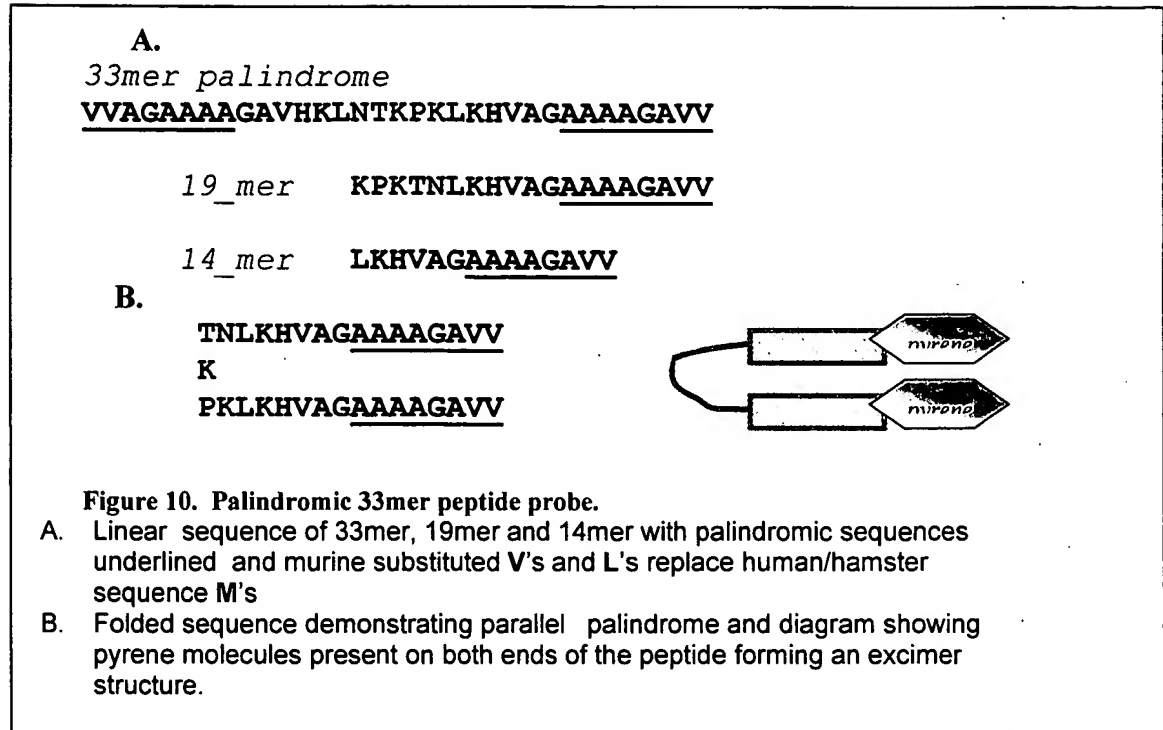


FIGURE 11

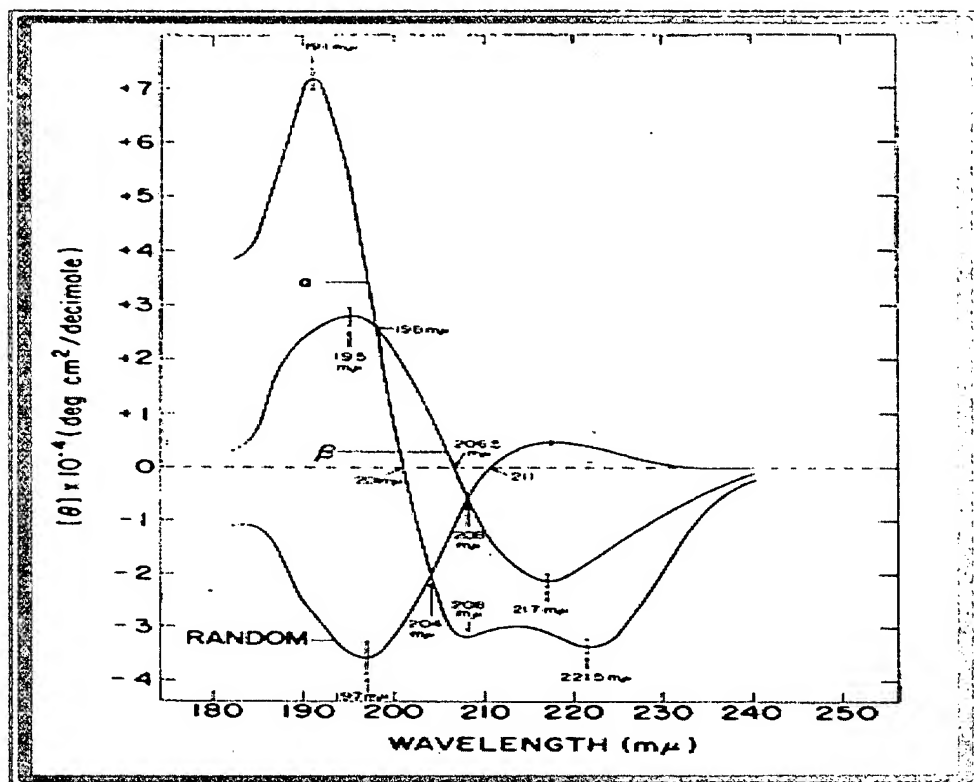


FIGURE 12

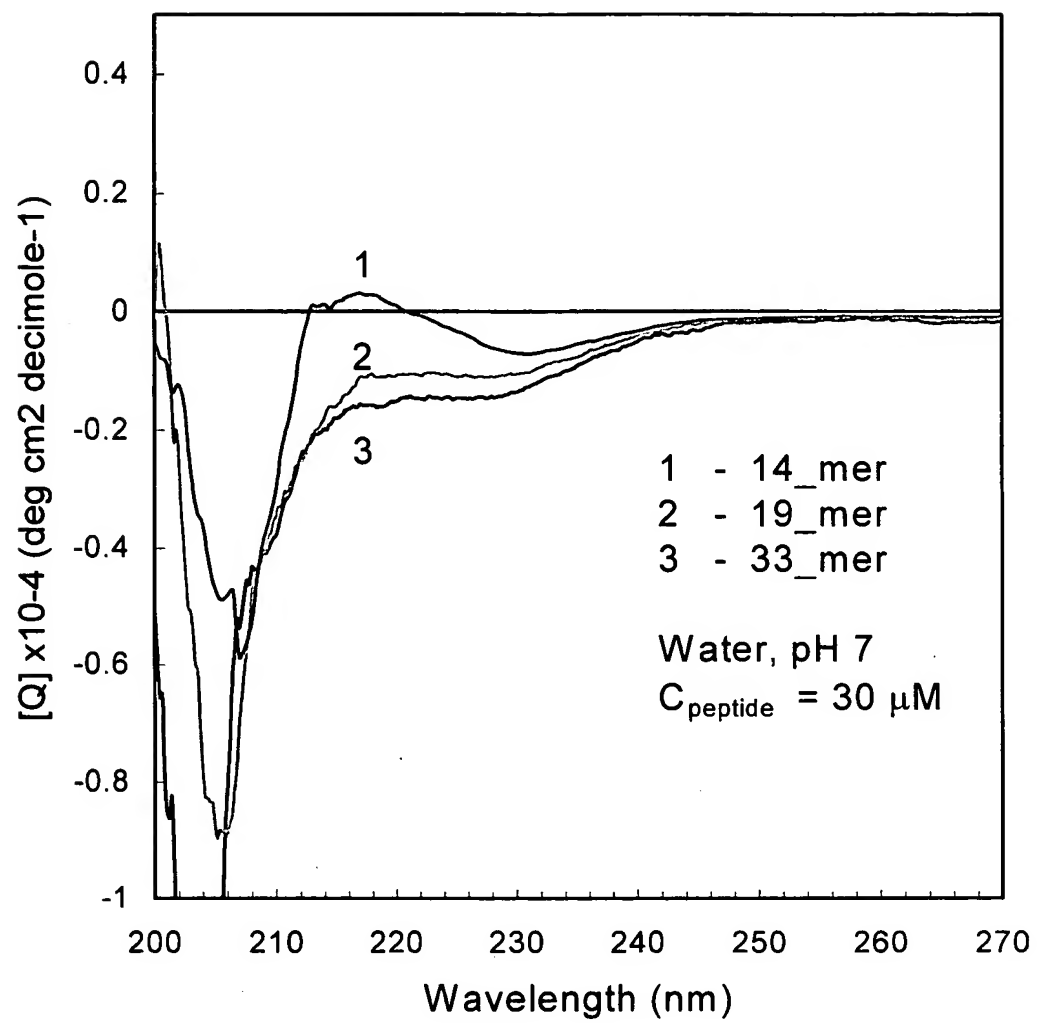


FIGURE 13

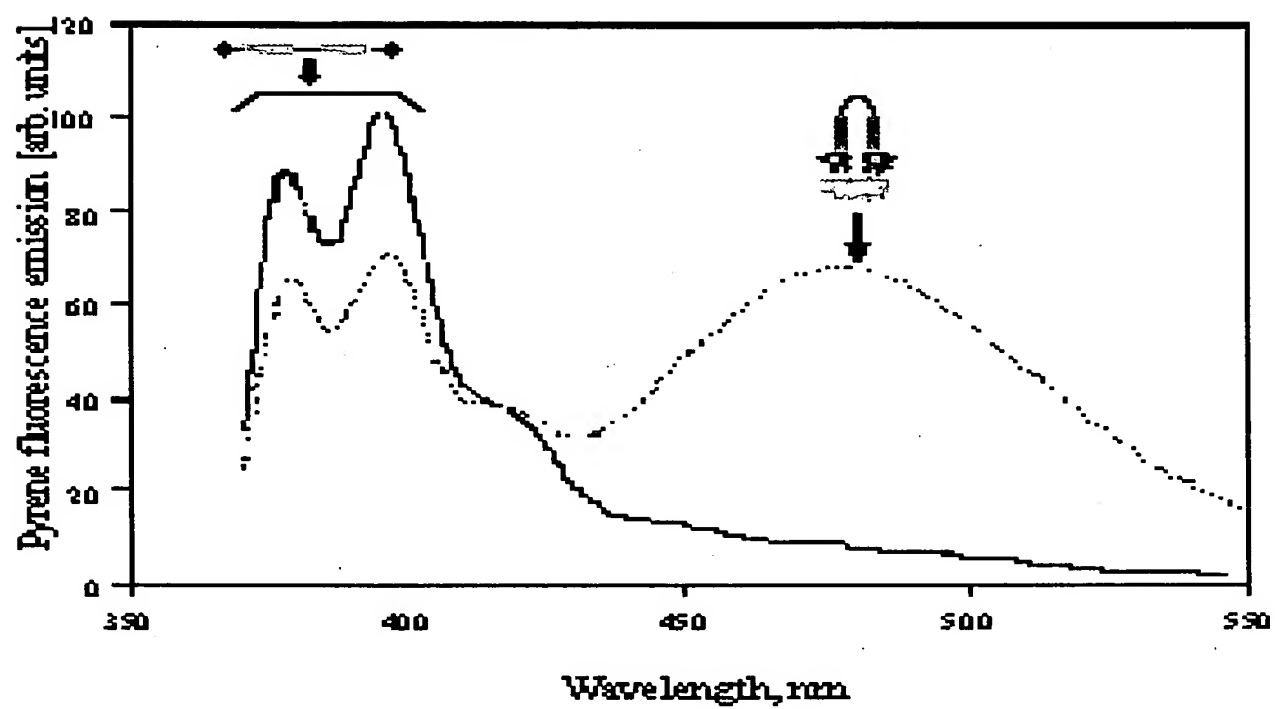


FIGURE 14

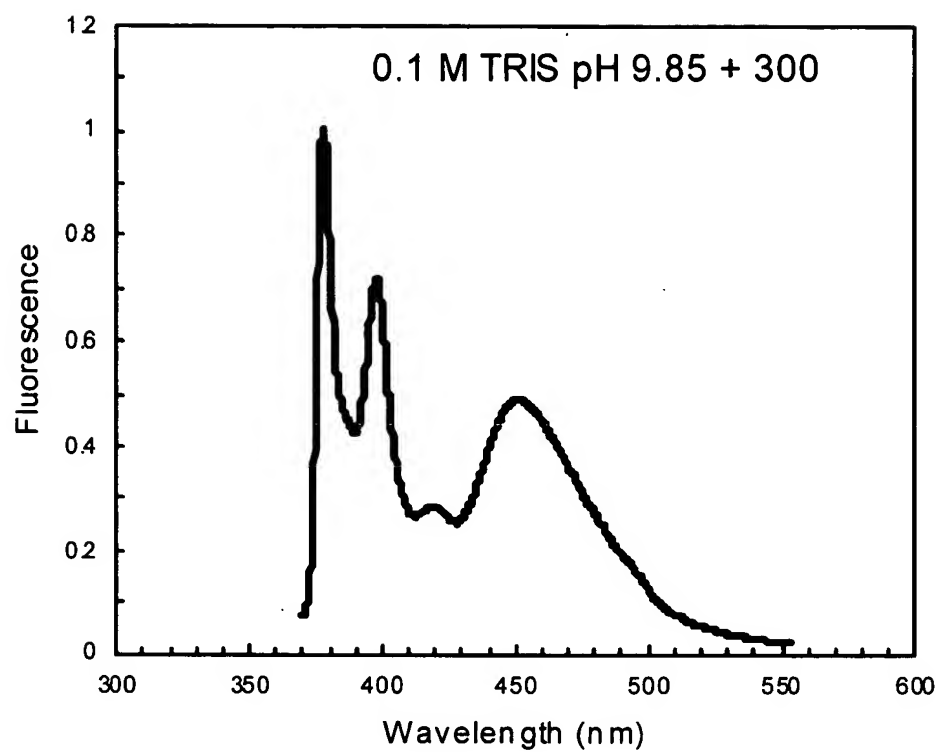


FIGURE 15

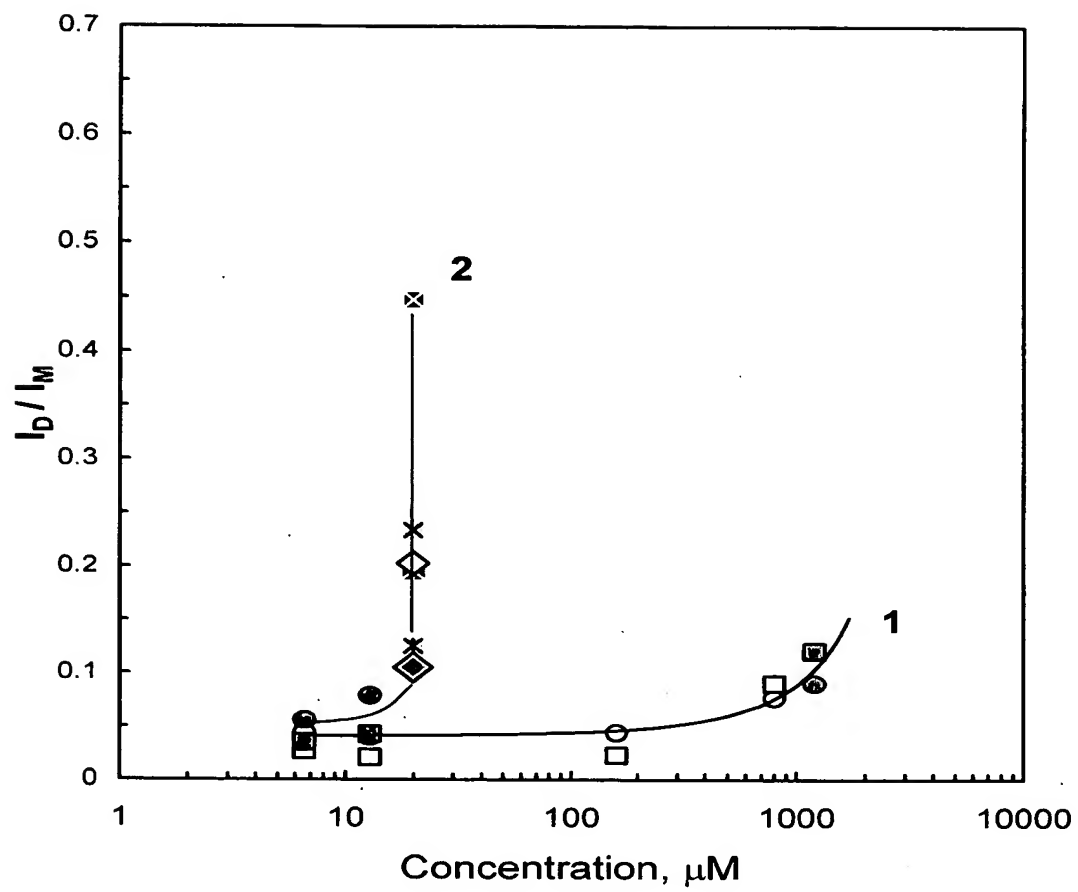


FIGURE 16

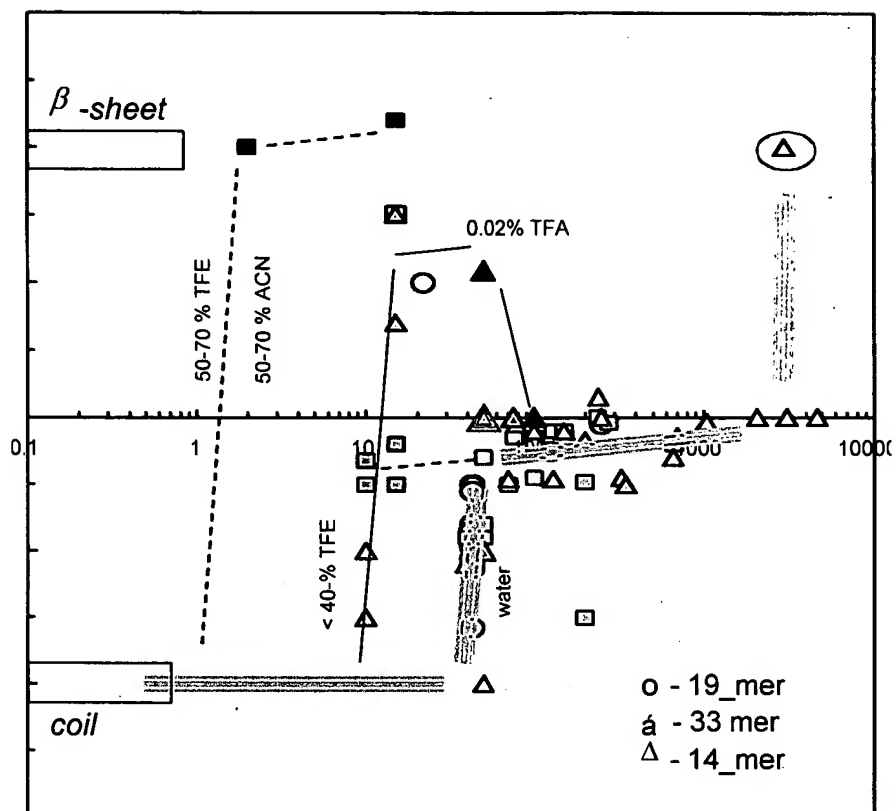


FIGURE 17

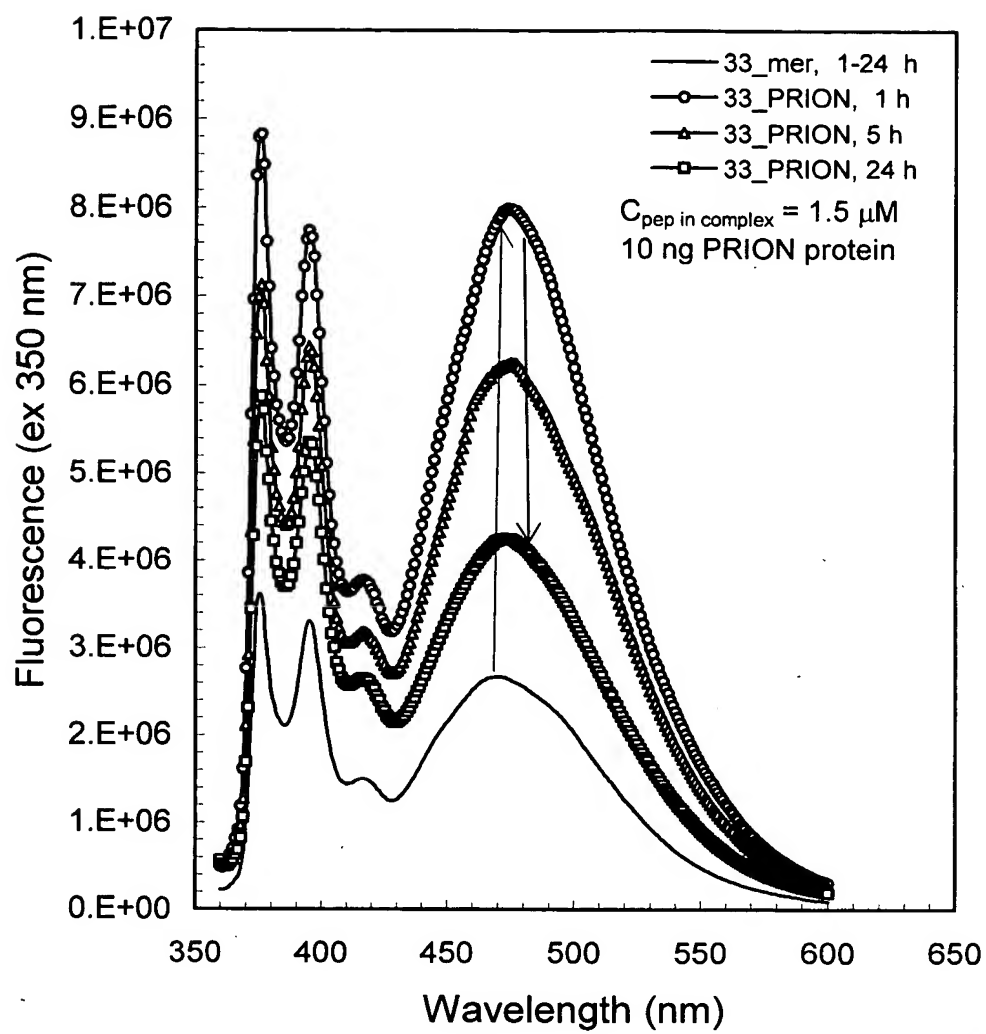


FIGURE 18

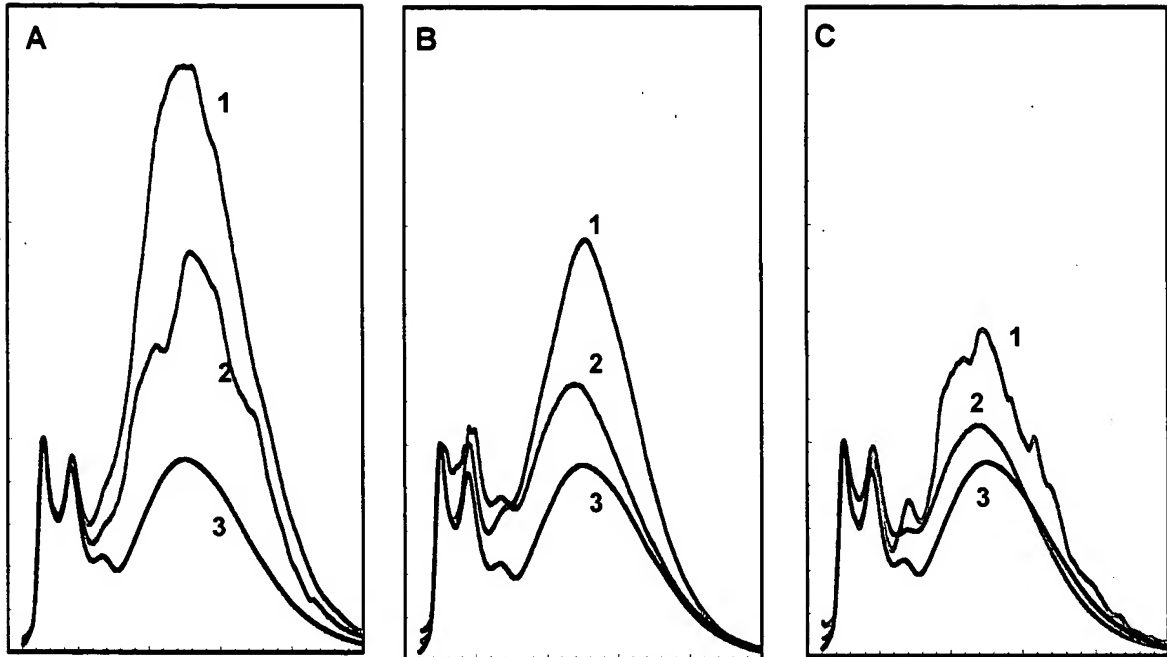


FIGURE 19

